



2009-11-17

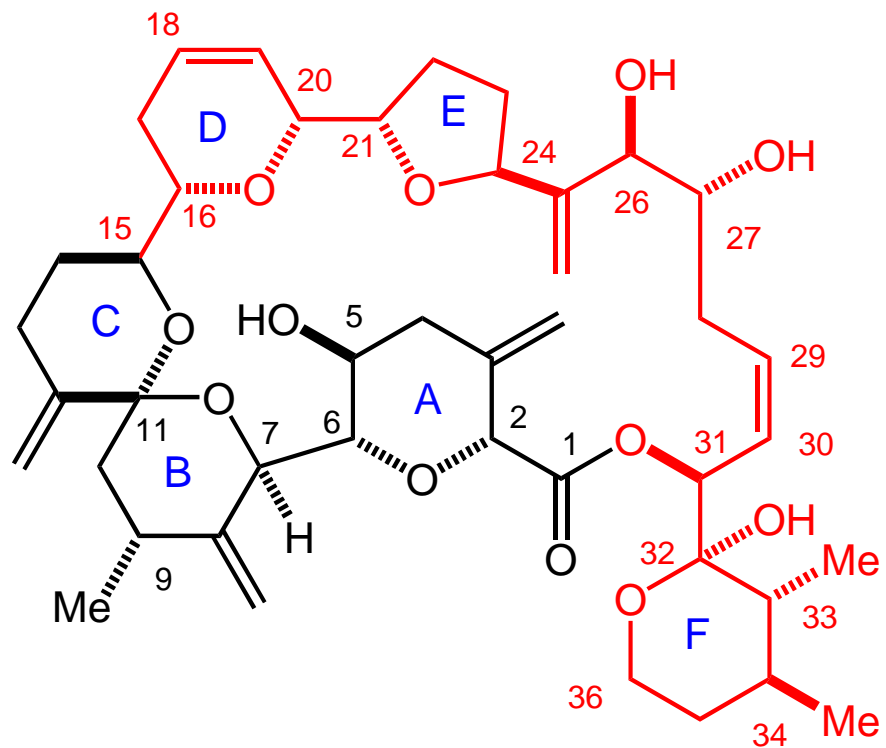
王躲生

检查: 段英

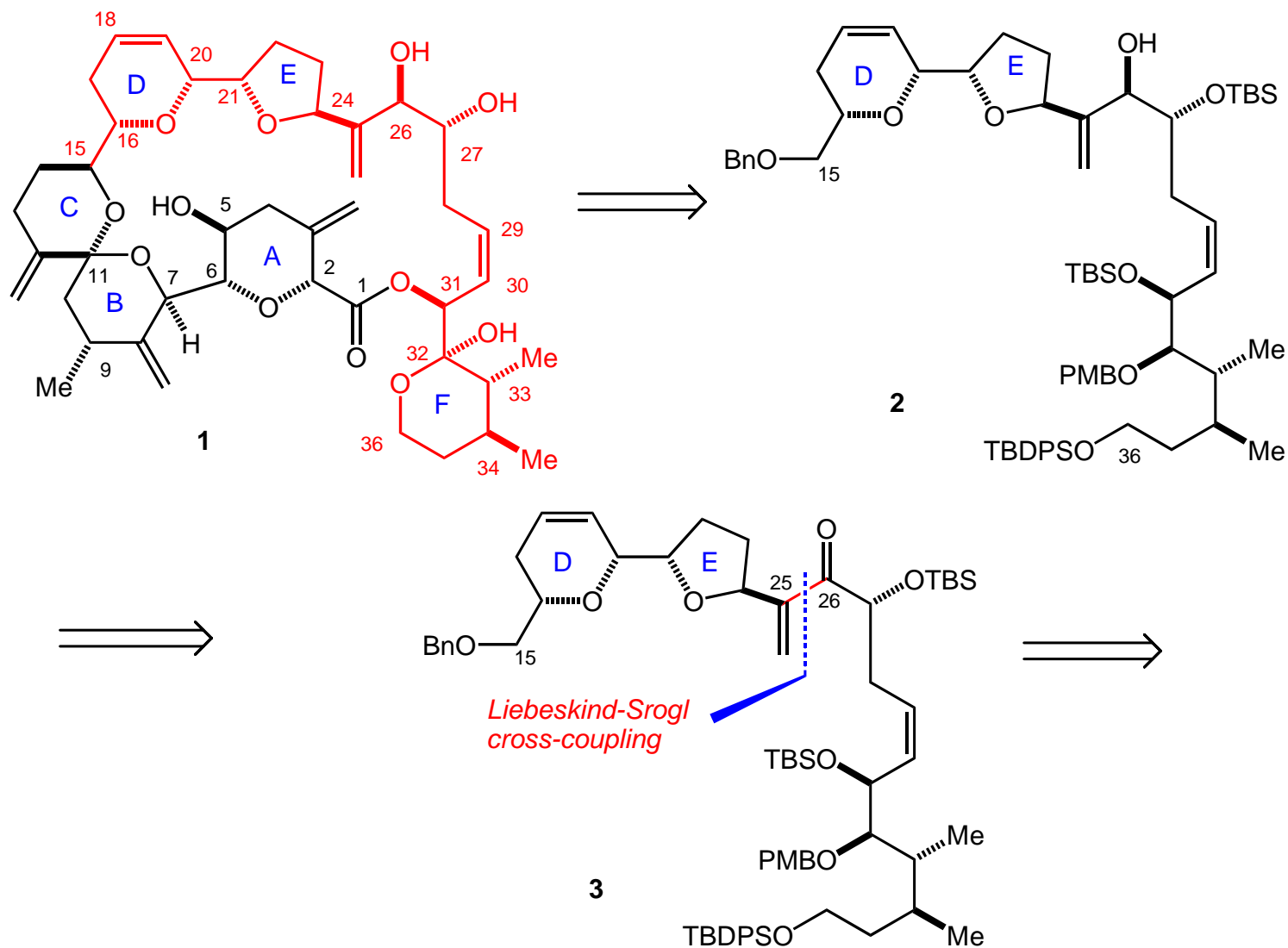
# Toward the Total Synthesis of Goniodomin A, An Actin-Targeting Marine Polyether Macrolide: Convergent Synthesis of the C15-C36 Segment

Sasaki, M.\*, *et al*  
*Org. Lett.* **2009**, *11*, 5274–5277.

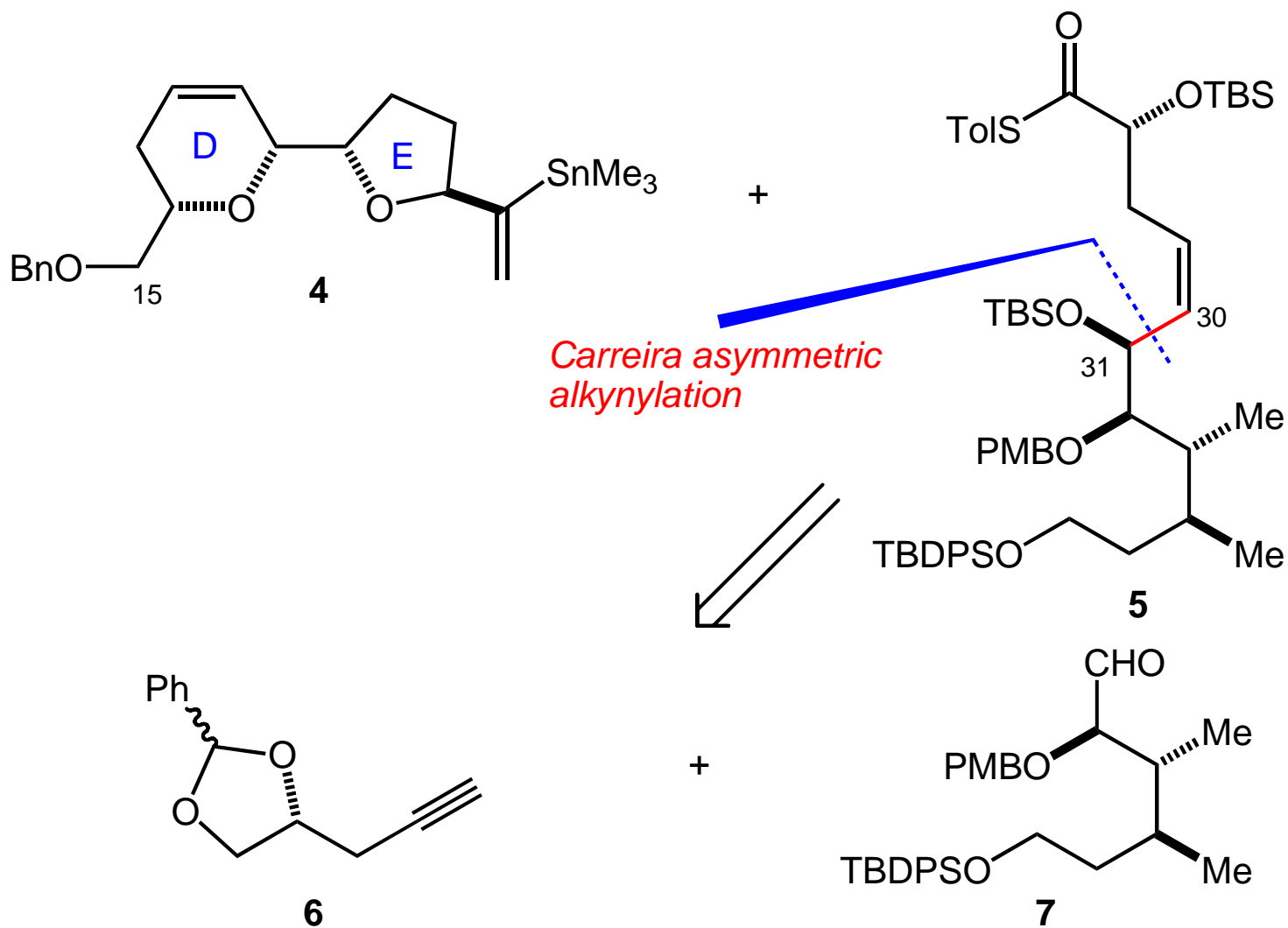
# Structure of goniodomin A (1)



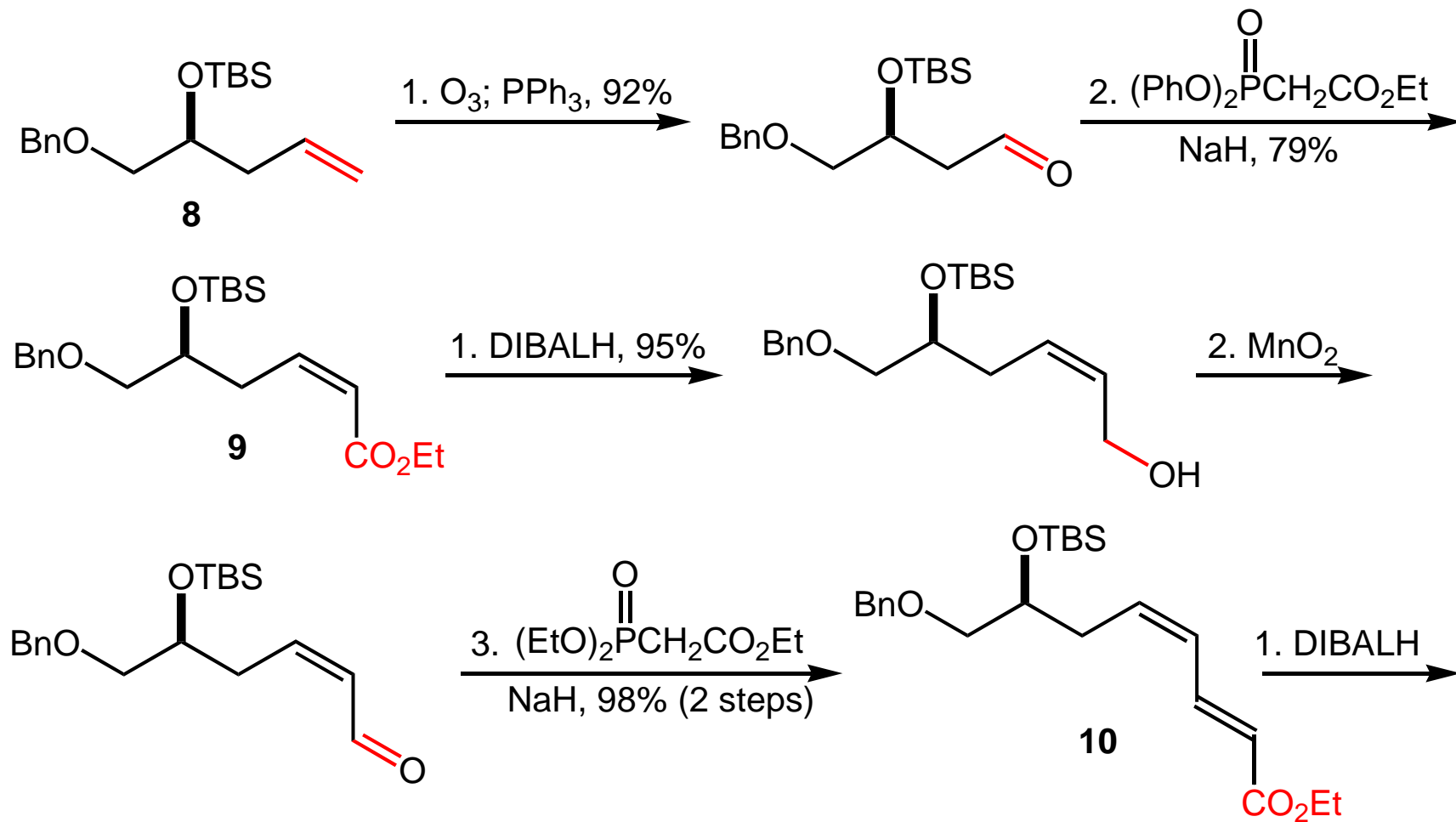
# Retrosynthetic Analysis:



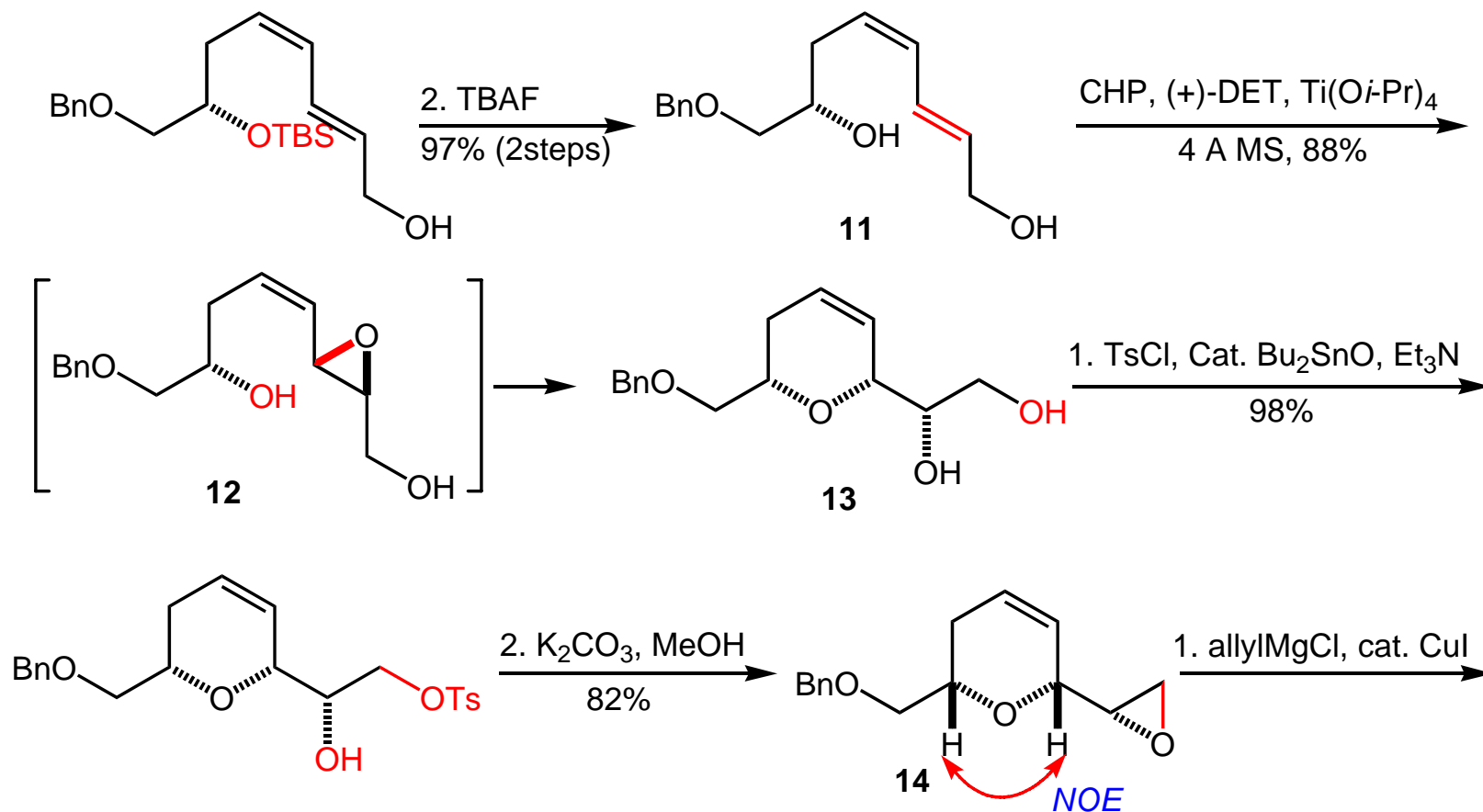
# Retrosynthetic Analysis:



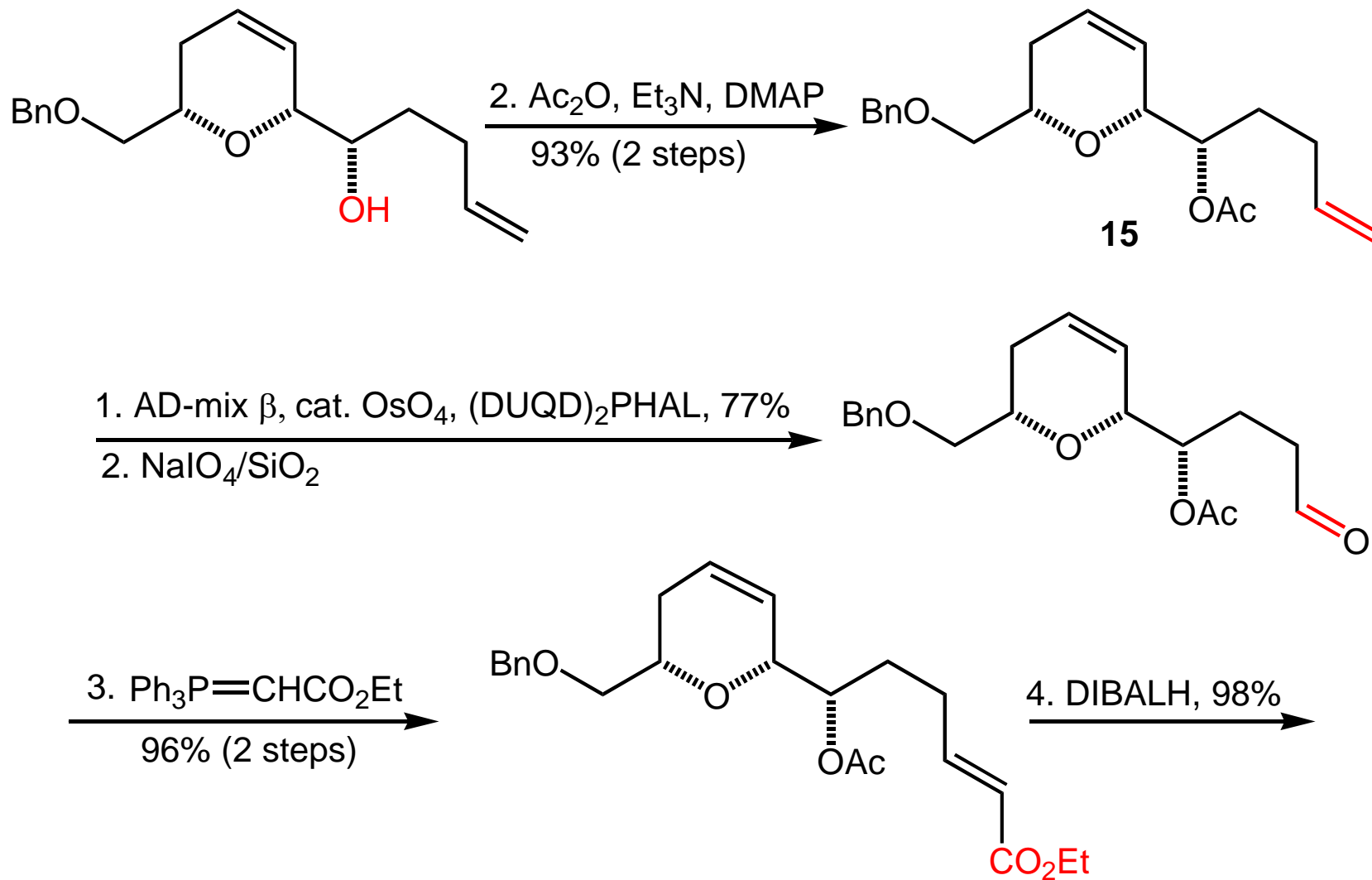
# Synthesis of Vinyl Stannane 4:



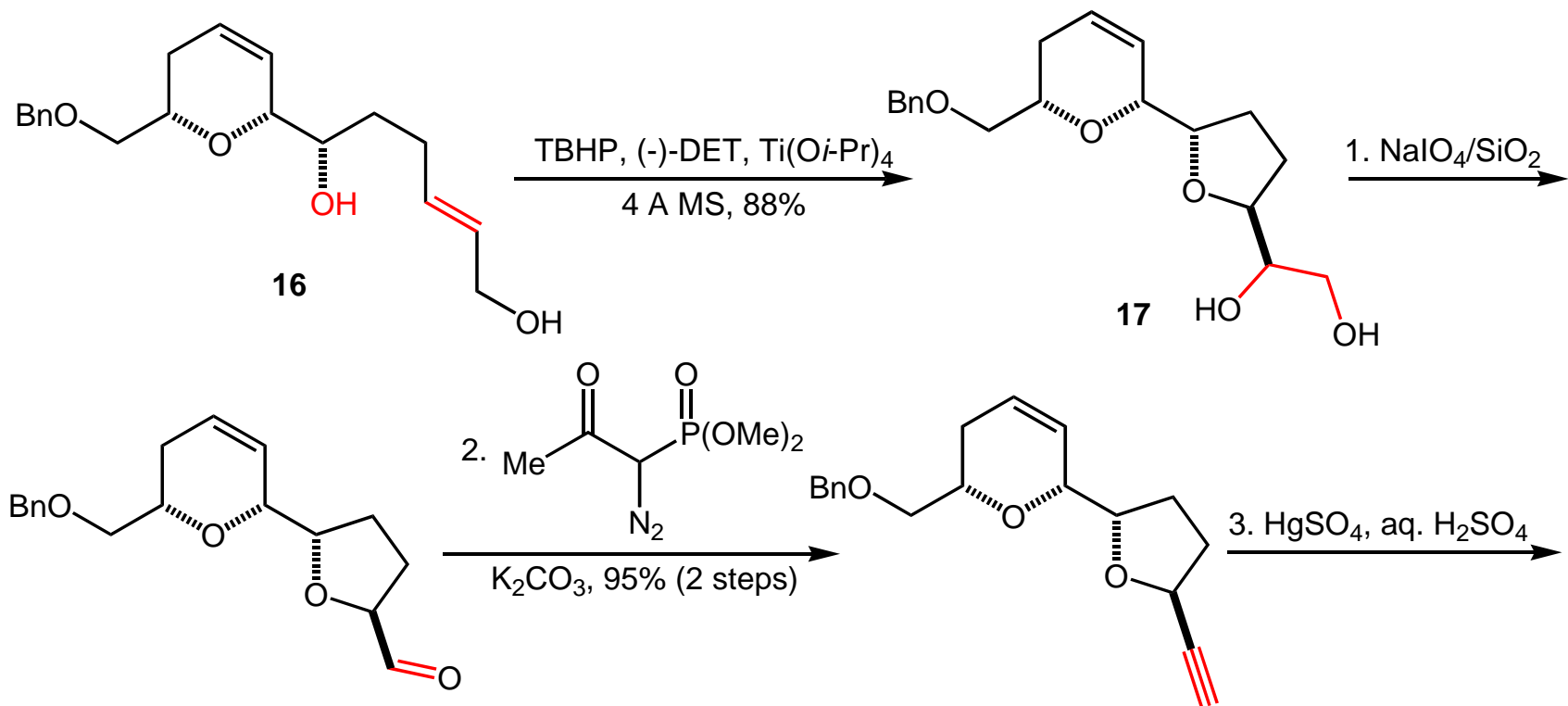
# Synthesis of Vinyl Stannane 4:



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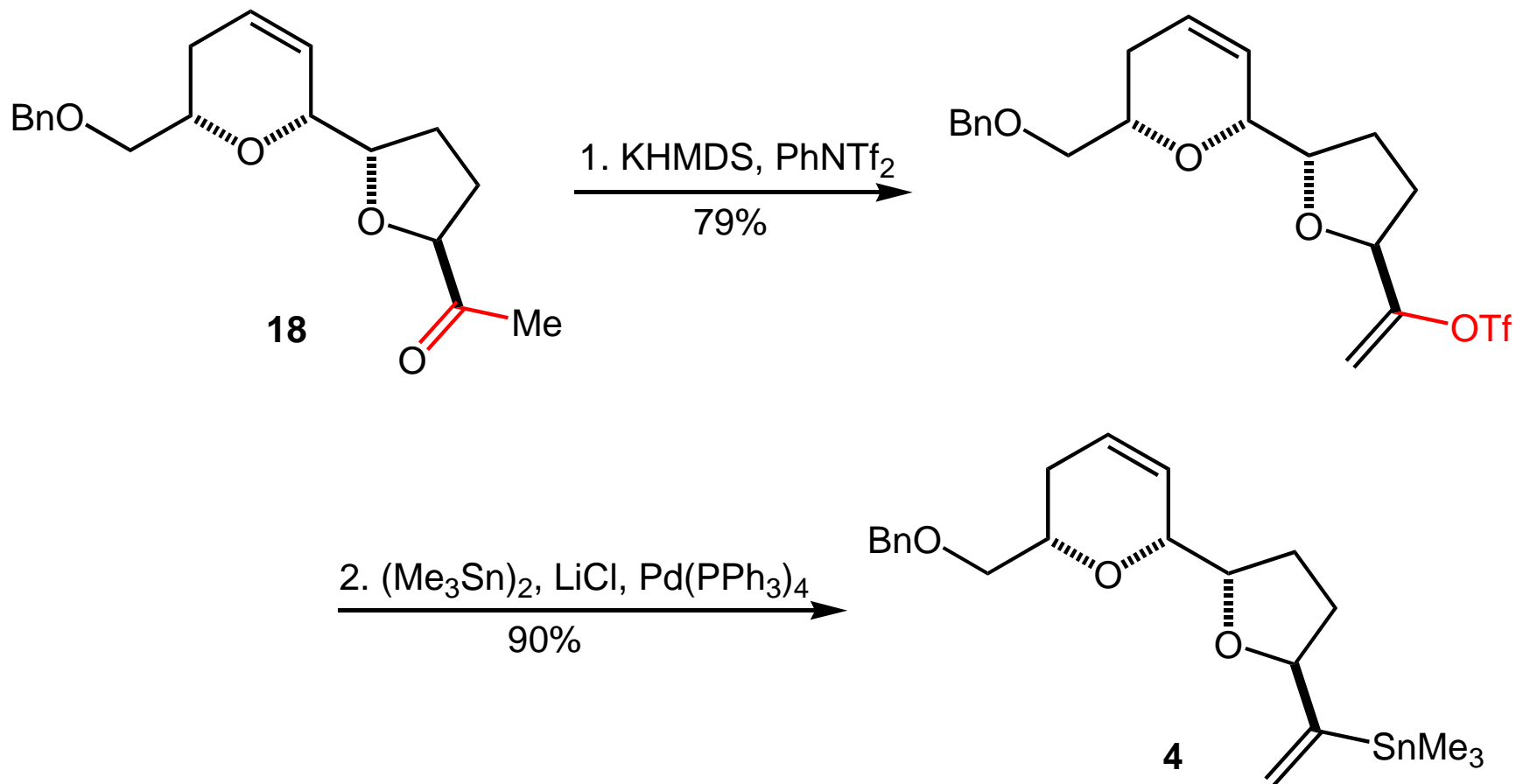


# Synthesis of Vinyl Stannane 4:

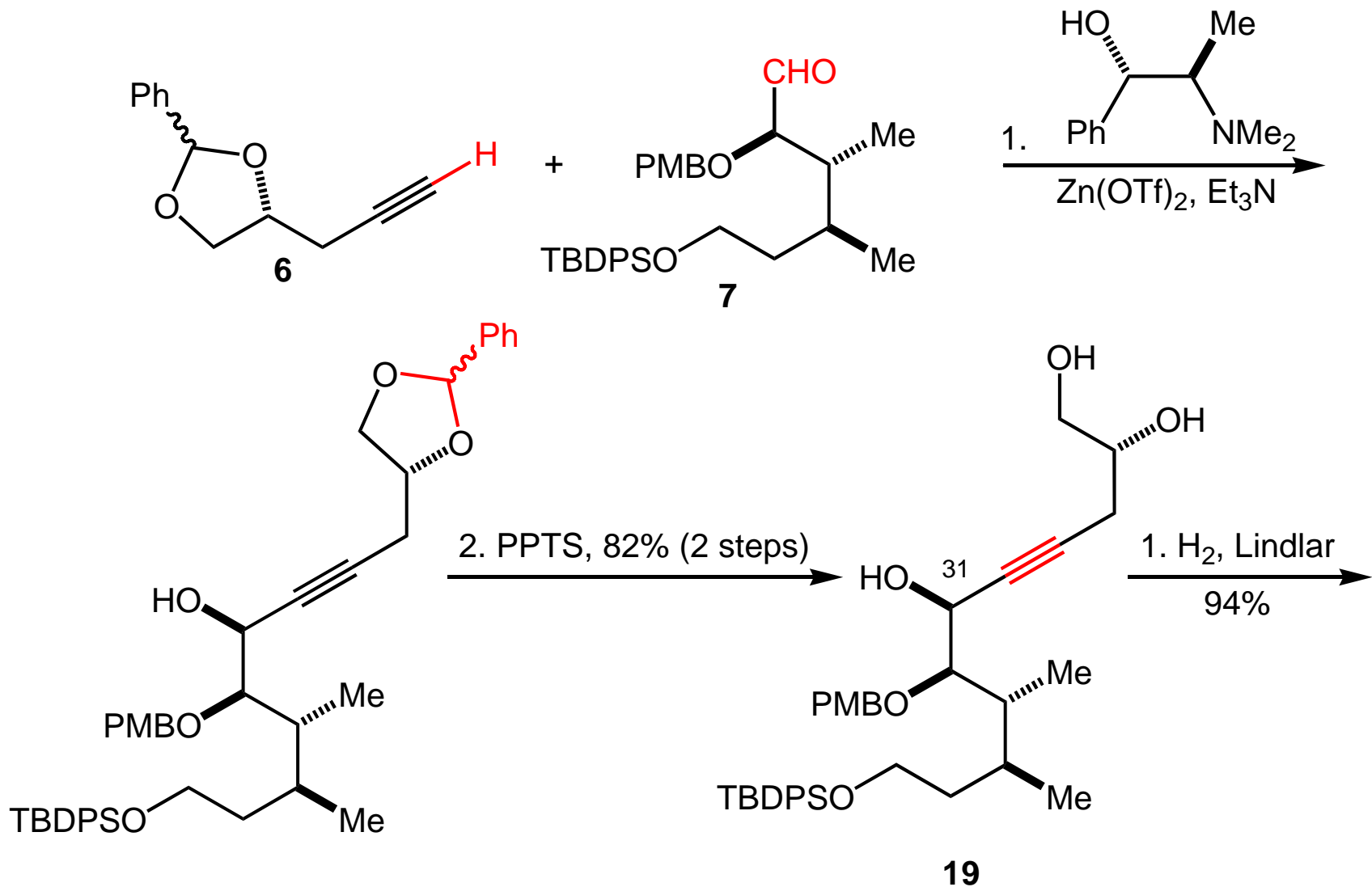




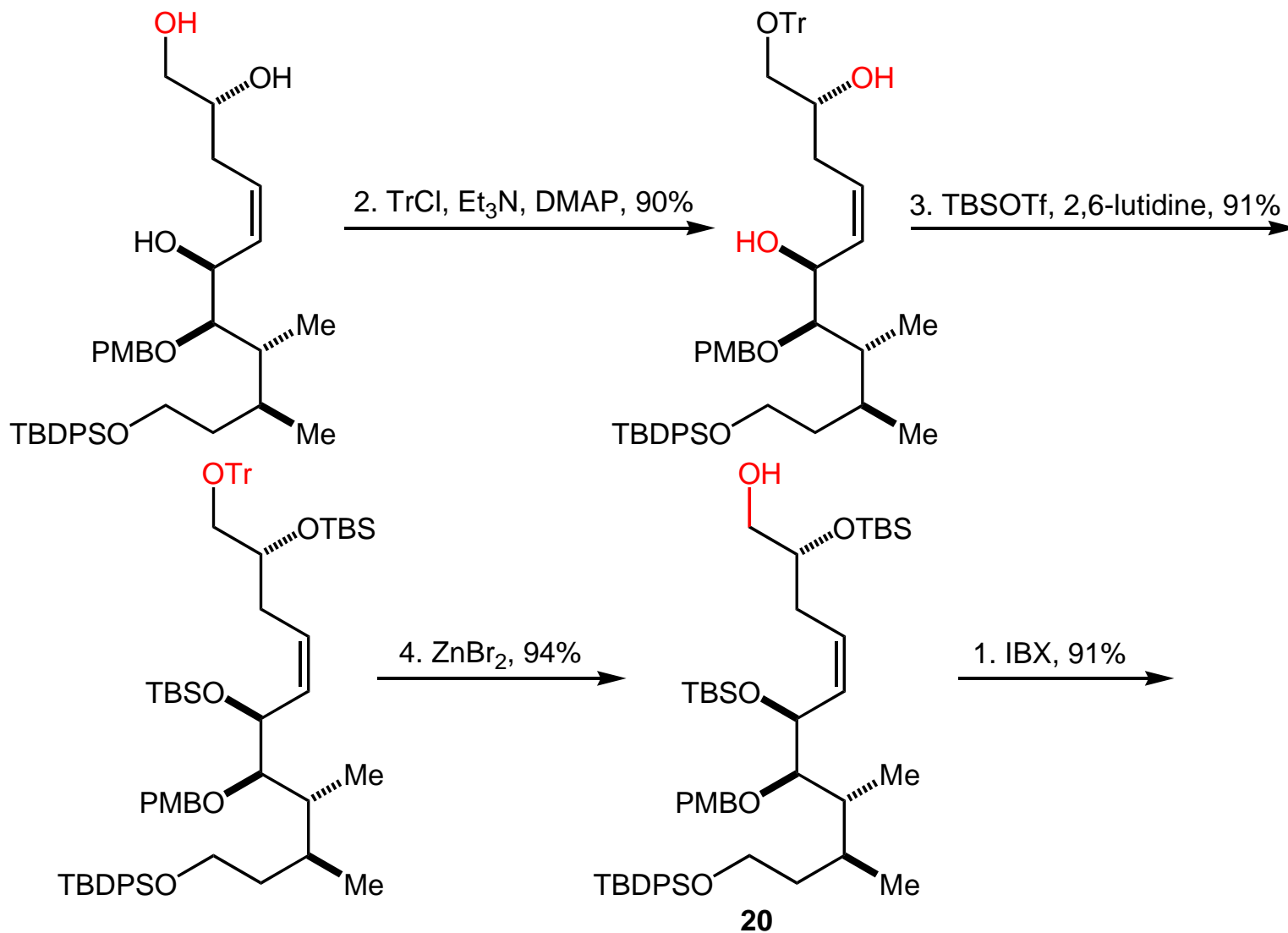
# Synthesis of Vinyl Stannane 4:



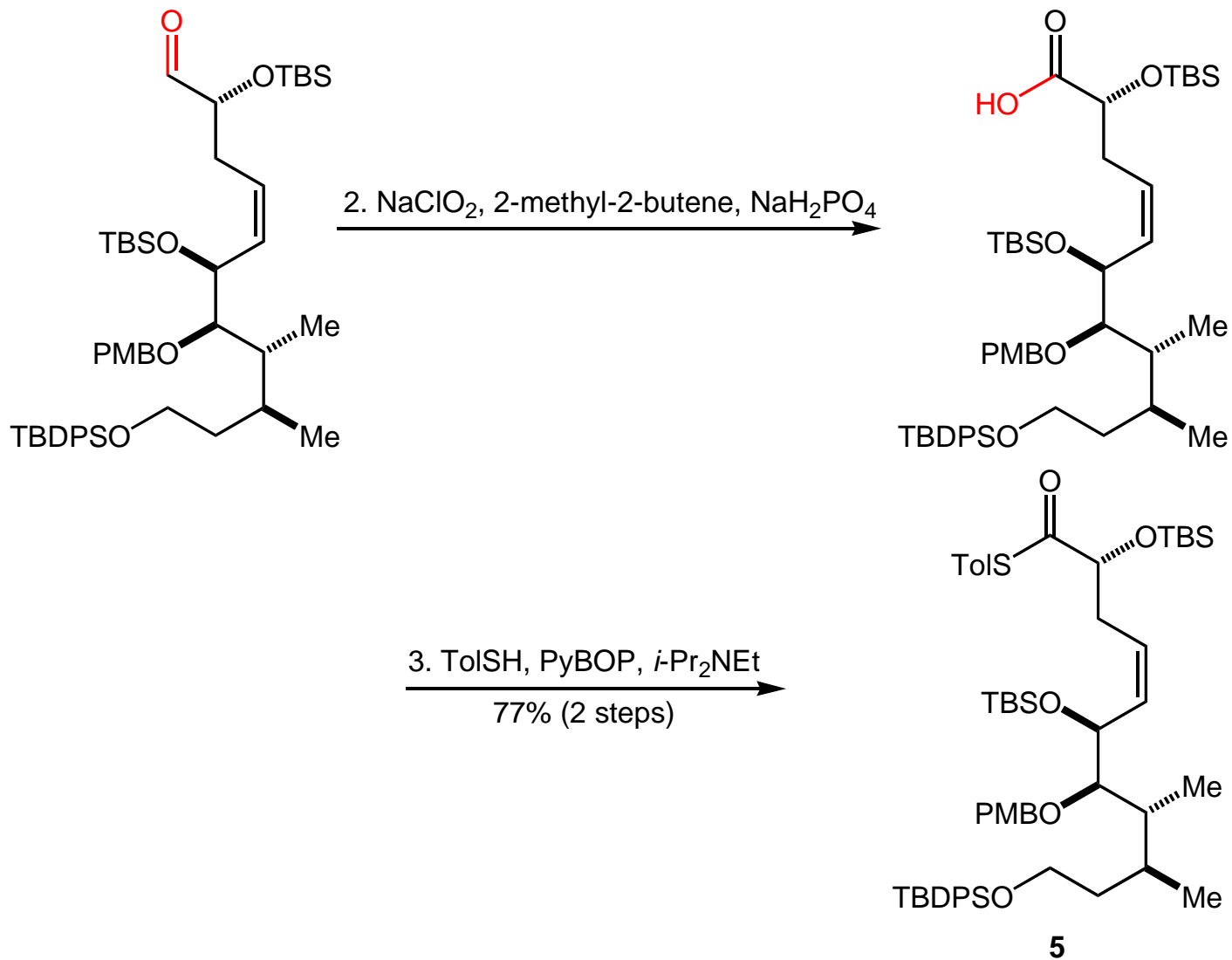
# Synthesis of Thiol Ester 5:



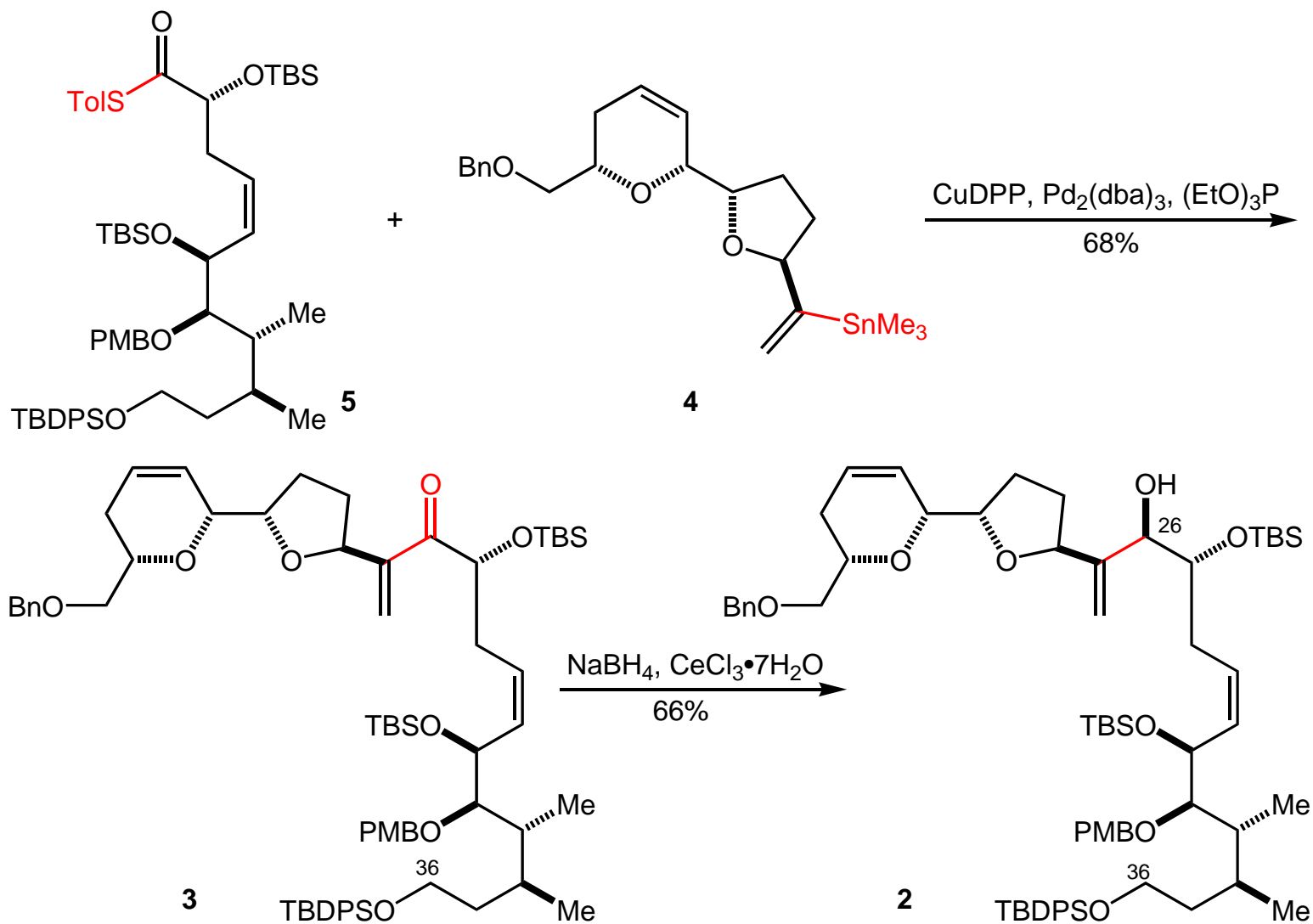
# Synthesis of Thiol Ester 5:



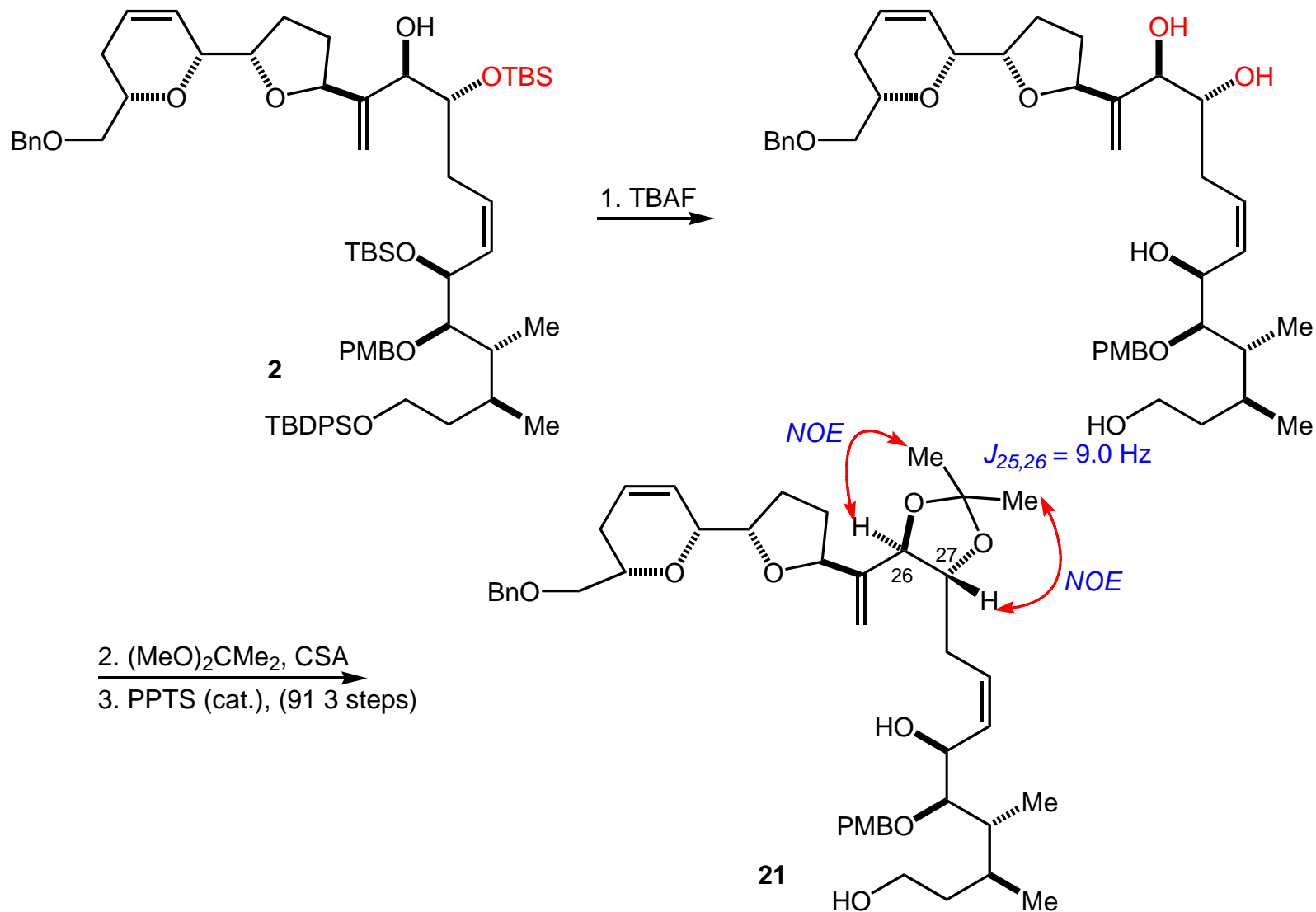
# Synthesis of Thiol Ester 5:




# Synthesis of C15-C36 Segment 2:



# Stereochemical Confirmation:



Goniodomin A (**1**) was isolated as a potent antifungal agent by Murakami and co-workers from the dinoflagellate *Alexandrium hiranoi* (formerly *Goniodoma pseudogoniaulax*) collected in a rock pool at Jogashima in Japan in 1988. More recently, it was reported that the dinoflagellate *Alexandrium monilatum* produced goniodomin A. The gross structure of goniodomin A was determined by Murakami and co-workers on the basis of the NMR studies to be a novel polyether macrolide, which is characterized by a spiroacetal ring (B/C-ring), an additional four oxacycles (A-, D-, E-, and F-rings), and 17 stereogenic centers embedded within a 36-carbon chain. We have recently defined the absolute configuration of goniodomin A on the basis of detailed 2D NMR studies and degradation experiments of the natural product, the synthesis of suitable model compounds for NMR spectroscopic comparisons, and by correlation with synthetic reference compounds.



In conclusion, we have developed a convergent synthetic route to the C15-C36 segment **2** of goniodomin A. Particularly noteworthy is a Pd(0)-catalyzed, Cu(I)-mediated Liebeskind-Srogl cross-coupling of complex fragments for the critical bond-forming step. Further studies toward the total synthesis of goniodomin A are currently underway in our laboratories and will be reported in due course.